

## What is claimed is:

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1. An oligomeric compound conjugated to a ligand that interacts with a protein.
  - 5 2. The oligomeric compound of claim 1 wherein said ligand binds to said protein.
  3. The oligomeric compound of claim 1 wherein said ligand is a drug moiety.
  4. The oligomeric compound of claim 3 wherein said  
10 drug moiety is, warfarin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, naproxen, dansylsarcosine, 2,3,5-triiodobenzoic acid, flufenamic acid, folinic acid, mycophenolic acid, a  
15 benzothiadiazide, chlorothiazide, a diazepam, indomethacin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.
  5. The oligomeric compound of claim 3 wherein said  
20 drug moiety is aspirin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, palmityl or carprofen.
  6. The oligomeric compound of claim 3 wherein said drug moiety is ibuprofen.
  7. The oligomeric compound of claim 1 wherein said protein is a cellular, serum or vascular protein.
  - 25 8. The oligomeric compound of claim 7 wherein said protein is a serum protein.
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9. The oligomeric compound of claim 8 having a  $K_d$  lower than 20  $\mu$ M with at least one serum protein.

10. The oligomeric compound of claim 8 wherein said serum protein is albumin, an immunoglobulin,  $\alpha$ -2-5 macroglobulin,  $\alpha$ -1-glycoprotein or a lipoprotein.

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11. The oligomeric compound of claim 1 further including a linking group attaching said ligand to said oligomeric compound.

12. The oligomeric compound of claim 11 wherein said linking group is 6-aminohexyloxy.

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13. The oligomeric compound of claim 1 wherein said compound is an oligonucleotide comprising a plurality of nucleosides connected by covalent internucleoside linkages.

14. The oligomeric compound of claim 13 wherein said linkages are phosphodiester linkages.

15. The oligomeric compound of claim 13 wherein said linkages are phosphorothioate linkages.

16. The oligomeric compound of claim 13 wherein said linkages are non-phosphorus containing linkages.

20 17. The oligomeric compound of claim 13 wherein at least one of said nucleosides bears a 2'-substituent group.

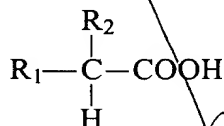
18. The oligomeric compound of claim 17 wherein said 2'-substituent group is O-alkylalkoxy.

19. The oligomeric compound of claim 18 wherein said

2'-substituent group is methoxyethoxy.

20. The oligomeric compound of claim 3 wherein said drug moiety is an arylpropionic acid.

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21. The oligomeric compound of claim 20 wherein said arylpropionic acid has the formula:



wherein:

- one of  $R_1$  and  $R_2$  is  $C_1$  to  $C_{12}$  alkyl and the other of  $R_1$  and  $R_2$  is aryl; or  
10 both  $R_1$  and  $R_2$  are  $C_1$  to  $C_{12}$  alkyl; or  
both  $R_1$  and  $R_2$  are aryl.

22. The oligomeric compound of claim 21 wherein said arylpropionic acid is chiral.

23. The oligomeric compound of claim 22 wherein said  
15 chiral arylpropionic acid has the S configuration.

24. The oligomeric compound of claim 22 wherein said chiral arylpropionic acid has the R configuration.

25. The oligomeric compound of claim 21 wherein said aryl groups are substituted or unsubstituted benzyl, phenyl,  
20 xylyl, naphthyl, toluyl, pyrenyl, anthracyl, phenanthryl, azulyl, phenethyl, cinnamyl, benzhydryl, and mesityl in said substituents are hydroxyl, alkyl, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, or alkyl, substituted alkyl, aryl, alkenyl, or alkynyl groups.

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26. A method of increasing the concentration of an oligonucleotide in serum comprising the steps of:

- (a) selecting a drug moiety that is known to bind to a serum protein;
- 5 (b) conjugating said drug moiety to said oligonucleotide to form a conjugated oligonucleotide; and
- (c) adding said conjugated oligonucleotide to said serum.

27. The method of claim 26 wherein said serum protein  
10 is albumin, an immunoglobulin,  $\alpha$ -2-macroglobulin,  $\alpha$ -1-glycoprotein or a lipoprotein.

28. The method of claim 26 wherein said serum protein is albumin.

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29. The method of claim 26 wherein said drug moiety is  
15 aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, naproxen, dansylsarcosine, 2,3,5-triiodobenzoic acid, flufenamic acid, folinic acid, mycophenolic acid, a benzothiadiazide, chlorothiazide, a diazepam, indomethacin,  
20 a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

30. The method of claim 26 wherein said drug moiety is aspirin, phenylbutazone, ibuprofen, suprofen, fenbufen,  
25 ketoprofen, (S)-(+)-pranoprofen, palmityl or carprofen.

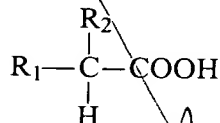
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31. The method claim 26 wherein said drug moiety is ibuprofen.

32. The method of claim 31 wherein said protein is albumin.

33. The oligomeric compound of claim 26 wherein said drug moiety is an arylpropionic acid.

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34. The oligomeric compound of claim 33 wherein said arylpropionic acid has the formula:



wherein:

one of  $R_1$  and  $R_2$  is  $C_1$  to  $C_{12}$  alkyl and the other of  $R_1$  and  $R_2$  is aryl; or

both  $R_1$  and  $R_2$  are  $C_1$  to  $C_{12}$  alkyl; or

both  $R_1$  and  $R_2$  are aryl.

35. The oligomeric compound of claim 34 wherein said arylpropionic acid is chiral.

36. The oligomeric compound of claim 35 wherein said chiral arylpropionic acid has the *S* configuration.

37. The oligomeric compound of claim 35 wherein said chiral arylpropionic acid has the *R* configuration.

38. The oligomeric compound of claim 34 wherein said aryl groups are substituted or unsubstituted benzyl, phenyl, xylyl, naphthyl, toluy, pyrenyl, anthracyl, phenanthryl, azulyl, phenethyl, cinnamyl, benzhydryl, and mesityl wherein said substituents are hydroxyl, alkyl, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, or alkyl, substituted alkyl, aryl, alkenyl, or alkynyl groups.

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39. A method of increasing the capacity of serum for an oligonucleotide comprising the steps of:

(a) selecting a drug moiety that is known to bind to a serum protein;

(b) conjugating said drug moiety to said oligonucleotide to form a conjugated oligonucleotide; and

(c) adding said conjugated oligonucleotide to said serum.

40. The method of claim 39 wherein said serum protein is a protein having a binding site for said drug moiety.

41. The method of claim 39 wherein said serum protein is a protein having a binding site for said oligonucleotide.

42. The method of claim 39 wherein said serum protein is a protein having a binding site for said oligonucleotide and a binding site for said drug moiety; wherein said binding site for said oligonucleotide is distinct from said binding site for said drug moiety.

43. A method of increasing the binding of an oligonucleotide to a portion of the vascular system comprising the steps of:

(a) selecting a drug moiety that is known to bind to a protein that resides, in part, in the circulating serum and in part in a non-circulating portion of the vascular system;

(b) conjugating said drug moiety to said oligonucleotide to form a conjugated oligonucleotide; and

(c) adding said conjugated oligonucleotide to said vascular system.

44. The method of claim 43 wherein said drug moiety is aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, naproxen, dansylsarcosine, 2,3,5-triiodobenzoic acid,

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flufenamic acid, folinic acid, mycophenolic acid, a benzothiadiazide, chlorothiazide, a diazepine, indomethacin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

5 45. The method of claim 43 wherein said drug moiety is aspirin, phenylbutazone, ibuprofen, suprofen, fenbufen, ketoprofen, (S)-(+)-pranoprofen, palmityl or carprofen.

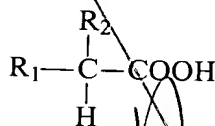
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46. The method claim 43 wherein said drug moiety is ibuprofen.

10 47. The oligomeric compound of claim 43 wherein said drug moiety is an arylpropionic acid.

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48. The oligomeric compound of claim 47 wherein said arylpropionic acid has the formula:



15 wherein:

one of  $R_1$  and  $R_2$  is  $C_1$  to  $C_{12}$  alkyl and the other of  $R_1$  and  $R_2$  is aryl; or

both  $R_1$  and  $R_2$  are  $C_1$  to  $C_{12}$  alkyl; or

both  $R_1$  and  $R_2$  are aryl.

20 49. The oligomeric compound of claim 48 wherein said arylpropionic acid is chiral.

50. The oligomeric compound of claim 49 wherein said chiral arylpropionic acid has the S configuration.

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51. The oligomeric compound of claim 49 wherein said

chiral arylpropionic acid has the *R* configuration.

52. The oligomeric compound of claim 48 wherein said aryl groups are substituted or unsubstituted benzyl, phenyl, xylyl, naphthyl, toluyl, pyrenyl, anthracyl, phenanthryl, azulyl, phenethyl, cinnamyl, benzhydryl, and mesityl wherein said substituents are hydroxyl, alkyl, alkoxy, alcohol, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, or alkyl, substituted alkyl, aryl, alkenyl, or alkynyl groups.

53. A method of promoting cellular uptake of an oligonucleotide in a cell comprising the steps of:

- (a) selecting a protein that resides on the cellular membrane and extends, at least in part, on the external side of said membrane;
- (b) selecting a drug moiety that is known to bind to said protein;
- (c) conjugating said drug moiety to said oligonucleotide to form a conjugated oligonucleotide; and
- (d) exposing said cell to said conjugated oligonucleotide.

54. The method of claim 35 wherein said protein is a cell surface integrin.

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